Capturing Alzheimer's disease genomes with induced pluripotent stem cells: prospects and challenges.

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Authors:	M A Israel, L S Goldstein
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Public Summary:

A crucial limitation to our understanding of Alzheimer's disease (AD) is the inability to study the disease in live, human neurons. Patient autopsies are limited in supply and only represent the aftermath of disease. Rodents designed to mimic AD lack important features of the disease, and they have not been useful in modeling the sporadic form of AD, which is the form that the vast majority of patients have. The recent discovery of induced pluripotent stem cells (iPSCs) provides a method to create a "disease in a dish," where diseases can be studied in the laboratory and new drugs can be tested using live, human samples. In this review, we discuss the genetics of AD patients and the potential for iPSCs to capture the genomes of these individuals and generate relevant cell types. Specifically, we examine recent insights into the ability of iPSCs to faithfully maintain the genomes of their respective patients, advances in the ability to make neural cells from iPSCs, and the ability of iPSCs to create neurodegenerative diseases in a dish.

Scientific Abstract:

ABSTRACT: A crucial limitation to our understanding of Alzheimer's disease (AD) is the inability to test hypotheses on live, patient-specific neurons. Patient autopsies are limited in supply and only reveal endpoints of disease. Rodent models harboring familial AD mutations lack important pathologies, and animal models have not been useful in modeling the sporadic form of AD because of complex genetics. The recent development of induced pluripotent stem cells (iPSCs) provides a method to create live, patient-specific models of disease and to investigate disease phenotypes in vitro. In this review, we discuss the genetics of AD patients and the potential for iPSCs to capture the genomes of these individuals and generate relevant cell types. Specifically, we examine recent insights into the genetic fidelity of iPSCs, advances in the area of neuronal differentiation, and the ability of iPSCs to model neurodegenerative diseases.

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